IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Jeffery J. Wheeler, *et al.*

Application No.: 09/566,700

Filed: May 8, 2000

For: LIPID NUCLEIC-ACID PARTICLES PREPARED VIA HYDROPHOBIC LIPID-NUCLEIC ACID COMPLEX INTERMEDIATE AND USE FOR GENE TRANSFER

Examiner: J. Epps

Art Unit: 1635

Declaration of Michael J. Hope, Ph.D. Under 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Michael J. Hope, Ph.D. state and declare as follows:

1. All statements herein made of my own knowledge are true, and statements made on information or belief are believed to be true and correct.

2. I am currently a Principal Scientist at Inex Pharmaceuticals Corporation (Burnaby, Canada), a biotechnology company whose primary focus is the development of cancer treatments that are based on its propriety drug delivery platform and that are more effective and have fewer side effects than conventional cancer treatments. I have been a Principal Scientist at Inex Pharmaceuticals Corporation since 1991. Prior to joining Inex Pharmaceuticals Corporation, I was a Vice-President of Research at Canadian Liposome Company (North Vancouver, Canada)

3. In addition, I am currently an Adjunct Professor in the Department of Medicine at the University of British Columbia (Vancouver, Canada). I have been a Professor, either an Adjunct Professor or an Assistant Professor, at the University of Columbia since 1989. I have been a Professor in both the Department of Medicine and the Department of Biochemistry.

4. In 1973, I graduated from the Queen Elizabeth College, University of London (London, England) with a Bachelor of Science degree in Biochemistry. In 1976, I was awarded my

Ph.D. in Membrane Biochemistry from the Royal Free Hospital School of Medicine, University of London (London, England). My graduate studies were carried out under the direction of Professor J.S. Lucy, Head of the Department of Biochemistry, Royal Free Hospital, School of Medicine, and my dissertation was entitled "Effects of Modification of Cholesterol Content on Chemically Induced Fusion in Erythrocytes."

5. Attached hereto as Exhibit A is a true copy of my *curriculum vitae* and a list of publications of which I am an author or co-author.

6. I have read and am familiar with the contents of the above-referenced patent application. In addition, I have read the Final Office Action, mailed May 21, 2002, received from the United States Patent & Trademark Office in the above-referenced patent application. It is my understanding that the Examiner is concerned that claims 42 and 44-71 are anticipated under 35 U.S.C. § 102(e) over U.S. Patent No. 5,820,873 ("Choi *et al.*"). For the reasons set forth herein, the Examiner's concern is overcome.

7. The presently claimed invention is directed, *inter alia*, to a method of introducing a nucleic acid into a cell, the nucleic acid being serum-stable and protected from degradation. More particularly, independent claim 42 reads as follows:

> 42. (Amended) A method of introducing a nucleic acid into a cell, said method comprising contacting said cell with a nucleic acid-lipid particle comprising a cationic lipid, a conjugated lipid that inhibits aggregation of particles, and a nucleic acid, ***wherein said nucleic acid in said nucleic acid-lipid particle is resistant in aqueous solution to degradation with a nuclease***.

8. The specification teaches methods of making lipid-nucleic acid particles via novel, hydrophobic nucleic acid-lipid intermediate complexes. Manipulation of these complexes in either detergent-based or organic solvent-based systems leads to nucleic acid-lipid particles, wherein the nucleic acid in the nucleic acid-lipid particles is protected from nuclease degradation.

9. It is my understanding that Choi *et al.* is cited by the Examiner as allegedly disclosing "particles that meet the structural limitations of the particles produced by the methods of the instant invention, [thus] the prior art particles are presumed to have the same functional properties as the particles produced by Applicant's claimed method" (*see*, page 3 of the Office Action).

10. I have reviewed the Choi *et al.* patent, and it is my opinion that Choi *et al.* do ***not*** teach (or even suggest) a nucleic acid-lipid particle, wherein the nucleic acid in the nucleic acid-lipid particle is resistant in aqueous solution to degradation with a nuclease as is recited in claim 42 and, in turn, dependent claims 44-71.

11. In fact, a perusal of Choi *et al.* reveals that in the Examples set forth therein methods for loading therapeutic agents, *e.g.*, vincristine, into liposomes are disclosed. More particularly, Example 9 sets forth the following loading (or encapsulation) method:

> The dry lipid was hydrated with 300 mM citrate buffer, pH 4.0. Following extrusion, the vesicles (100 mg/mL) were added to a solution of vincristine (Oncovin; 1 mg/ml) to achieve a drug:lipid ration of 0.1:1. The exterior pH of the liposome/vincristine mixture was raised to pH 7.0-7.2 by titration with 500 mM sodium phosphate and immediately the sample was heated to 60°C for 10 minutes to achieve encapsulation of the vincristine.

See, Example 9, column 21, lines 11-18. Example 10 sets forth a similar loading/encapsulation procedure for loading vincristine into liposomes (*see*, Example 10, column 21, line 62 through column 22, line 9).

12. It is my opinion that if the loading methods disclosed by Choi *et al.* were used to load a nucleic acid into a liposome, such methods would ***not*** result in the nucleic acid-lipid particles of the present invention, wherein the nucleic acid in the nucleic acid-lipid particle is resistant in aqueous solution to degradation with a nuclease. Instead, using the loading methods disclosed by Choi *et al.*, the nucleic acid would not be fully encapsulated in the liposome and, thus, it would be susceptible in aqueous solution to degradation with a nuclease.

13. As such, in my opinion, the Choi *et al.* patent does ***not*** teach (or even suggest) the method recited in claims 42 and 44-71 because Choi *et al.* do ***not*** teach (or even suggest) (1) nucleic acid-lipid particles, wherein the nucleic acid in the nucleic acid-lipid particles is resistant in aqueous solution to degradation with a nuclease, or (2) methods for making such nucleic acid-lipid particles.

I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements

are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: Sep. 20th, 2002

M. J. Hope

Michael J. Hope, Ph.D.

Curriculum Vitae

Date: September 20, 2002 **Initials:**

SURNAME: HOPE

FIRST NAME: Michael

MIDDLE NAME(S): John

DEPARTMENT: Research

PRESENT RANK: Principal Scientist

POST-SECONDARY EDUCATION

University or Institution	Degree	Subject Area	Dates
Queen Elizabeth College, University of London, England	B.Sc.	Biochemistry	1970-73
Royal Free Hospital School of Medicine University of London, England	PhD	Membrane Biochemistry (cholesterol and membrane fusion)	1973-76

Special Professional Qualifications

PhD - Effects of modification of cholesterol content on chemically induced fusion in erythrocytes (Under the direction of Professor J.A. Lucy, Head of Department of Biochemistry, Royal Free Hospital, School of Medicine))

EXHIBIT A

EMPLOYMENT RECORD

University, Company or Organization	Rank or Title	Dates
Inex Pharmaceuticals Corp., Burnaby, British Columbia, Canada	Principal Scientist	1991-Present
Department of Medicine, University of British Columbia, Vancouver, Canada	Adjunct Professor	1998-Present
Department of Medicine, University of British Columbia, Vancouver, Canada	Assistant Professor	1991-1997
Department of Biochemistry, University of British Columbia, Vancouver, Canada	Adjunct Professor	1989-1991
Canadian Liposome Company, North Vancouver, BC, Canada	Vice President Research	1987-1991
Department of Biochemistry, University of British Columbia, Vancouver, Canada	Research Associate	1978-87
European Molecular Biology Organization, Unviersity of Utrecht, The Netherlands	Research Fellow	1977-78
Dutch Ministry of Education and Science Scholar at University of Utrecht, The Netherlands	Research Fellow	1976-77

(b) At UBC

Rank or Title	Dates
Research Assistant	1978 - 1980
Research Associate	1980 - 1987
Honorary Research Associate	1988 - 1989
Adjunct Professor (Biochemistry)	1989 - 1991
Assistant Professor (Medicine/Dermatology)	1991 - 1997
Associate Member (Biochemistry)	1992 - present
Adjunct Professor (Medicine/Dermatology)	1998 - present

TEACHING

Courses Taught at UBC

Session	Course Number	Scheduled Hours	Class Size	Hours Taught			
				Lectures	Tutorial	Labs	Other
1979-80	Bioc 403 Enzymology	36	~ 100	18			
1980	Bioc 508 Biomembranes	48	~ 20	2			
1981	Bioc 509 Biomembranes	48	~ 20	4			
1982-84	Bioc 400 Human Biochem.	72	~ 100 - 200	4			
1983-85	Bioc 508 Biomembranes	48	~ 20	4			
1987 - present	Bioc 509 Biomembranes	48	~ 20	9 - 18			Variable teaching load
1980 - present	Bioc 449	72	~ 5 total			>72 each	Supervision of Honors Thesis
1988 - present	Bioc 302. General Biochem.	36	~ 200 - 400	9 - 18			Min. 6 double lectures max.12.
1991	4th year U. of Victoria Membrane biochemistry	48	~ 20	8			Invited to teach membrane course
1998 - 2001	MedG521 Path531	36	~ 20	6			

Graduate Students Supervised

Student Name	Program Type	Year		Principal Supervisor	Co-Supervisor
		Start	Finish		
S. Eastman	PhD	1987	1991	P. Cullis	M. Hope
R. Harrigan	PhD	1988	1993	P. Cullis	M. Hope
A. Bailey	PhD	1992	1996	P. Cullis	M. Hope
K. Mok	PhD	1993	1997	P. Cullis	M. Hope
W. Rodrigueza	PhD	1988	1994	M. Hope	none
S. Klimuk	PhD	1992	1998	M. Hope	none
W. Mok	MSc	1995	1997	M.Hope	none
S. Raney	PhD	1996	2001	M. Hope	none

Continuing Education Activities

Management courses at the Justice Institute of B.C.

1. Basic Supervisory Program (7 hours) (1995)
2. Conflict Resolution (7 hours) (1996)
3. Problem Solving and Decision Making (7 hours) (1996)
4. Leadership and Teamwork, Empowerment and Delegation (7 hours) (1996)

Project Management

Pape Management Consultants (30 hours) (1996)
MS-Project (Advanced) Drake Computer Training (8 hours) (1996)
Lab to Leadership (24 hours) (1998)

Research or equivalent grants (grants were obtained competitively (C) or non-competitively (NC))

#	Granting Agency	Subject	COMP	$ Per Year	YEAR	Principal Invest(s)	Co-Invest(s)
1	B.C. Heart and Stroke Foundation	Liposomes and the regression of atherosclerosis	C	$26,000	89/90	Hope	Cullis
2	B.C. Heart and Stroke Foundation	Liposomes and the regression of atherosclerosis	C	$26,000	90/91	Hope	Pritchard
3	B.C. Health Development Fund	Technetium labelled liposomes (awarded grant but did not take it due to other commitments)	C	$22,000	90/91	Hope	
4	B.C. Science Council.	Liposomal anticancer pharmaceuticals - Funds matched by Canadian Liposome Co.	C	$196,000	89/90 90/91	Cullis Hope Bally Madden Mayer	
5	DRES (Defence Research Establishment Suffield, Alberta)	Encapsulation of antibiotics	NC	$50,000	91/92	Hope	
6	B.C. Health Development Fund	Lipid based topical delivery systems	C	$15,000	91/92 92/93	Hope	Kitson
7	Hoechst (Pharmaceutical Company)	Topical formulation of corticosteroids	NC	$30,000	92/93	Hope	Kitson
8	B.C. Health Development Fund	Multiple skin diffusion apparatus	C	$13,200	92/93	Hope	
9	Johnson & Johnson (Pharmaceutical Company)	Lung surfactant formulation	NC	$27,500	91/92	Hope	Madden
10	INEX Pharmaceuticals Corp.	Formulation of drugs, antisense and genes for topical and systemic treatment of skin diseases.	NC	$100,000	92/93 93/94 94/95 95/96	Hope	
11	Sunstar Inc. (Skin Care Products - Japan)	Liposome training program for Company Scientist	NC	$36,500	92/93	Hope	Cullis

#	Granting Agency	Subject	COMP	$ Per Year	YEAR	Principal Invest(s)	Co-Invest(s)
12	Lipex Biomembranes	Development of liposome technology	NC	$9,000	92/93 93/94 94/95 95/96	Hope	
13	IRAP (National Research Council matching fund grant)	Development of a non-viral gene delivery system for the treatment of cystic fibrosis.	C	$175,000	94/95 95/96	Hope	
14	B.C. Science and Technology Development Fund	Novel biopharmaceuticals for intracellular delivery - funds matched by Inex.	C	$200,000	95/96 96/97	Hope (PI for antisense and gene therapy)	
15	Medical Research Council	Gene Therapy	C	$60,000	94/97	Bally Hope	
16	NSERC Technical Partnership Program (TPP grant)	Development of fusogenic delivery systems for the intracellular delivery of antibiotics.	C	$80,000	96/97 97/98 98/99	Hope Finlay	
17	B.C. Science Council GREAT award.	Scholarship funding for S. Klimuk, graduate student - antisense therapy and delayed type hypersensitivity	C	$17,000	94/95 95/96 96/97	Hope	
18	B.C. Science and Technology Fund.	Development of novel antibiotic delivery systems.	C	$100,000	96/97	Hope	
19	B.C. Science Council GREAT award.	Scholarship funding for W. Mok, graduate student - Protein drug delivery	C	$17,000	96/97 98/99 00/01	Hope	
20	DRES (Defence Research Establishment Suffield, Alberta)	Antiviral activity of polyIC, a synthetic double RNA polymer.	NC	$33,333	97/00	Hope	
21	B.C. Science Council GREAT award.	Scholarship funding for S. Raney, graduate student – Topical ODN delivery	C	$17,000	97/98 99/00 00/01	Hope	
22	Medical Research Council	Gene Therapy	C	$60,000	97/00	Bally Hope	

(c) Invited Presentations

#	TITLE	LOCATION	DATE
1.	Cholesterol and lipid induced membrane fusion	University of Utrecht, Utrecht, The Netherlands.	February 1977
2.	Role of nonbilayer lipid structures in membrane fusion	Royal Free Hospital, School of Medicine, University of London, U.K	December 1980
3.	Membrane fusion	University of B.C., Vancouver, Canada	January 1981
4.	Nonbilayer lipid structure and lipid fusion processes	Gordon research Conference on transport phenomena in lipid bilayers and biological membranes. Tilton, NH, USA	August 1981
5.	Liposomes and cancer chemotherapy	Canadian Association of Hopsital Pharmacists Toronto, ON, Canada.	February 1987
6.	Liposomes and drug delivery	Cooper Pharmaceutical Laboratories, San Francisco, CA, USA.	June 1987
7.	Liposomes and topical drug delivery	Canadian Society for Investigative Dermatology, Japer, AL, Canada	February 1991
8.	Therapeutic applications of lipids	Dept. Biochemistry, University of BC, Vancouver, BC Canada	March 1992
9.	Membrane fusion and intracellular drug delivery	ISIS Pharmaceuticals, San Diego, CA, USA	January 1993
10.	Liposomal ciprofloxacin	DCIEM Liposome Conference, Toronto, ON, Canada	October 1993
11.	Liposomes: possible therapeutic application in the management of atherosclerosis?	Lipoprotein Research Conference, Cecil Green, University of BC, Vancouver, Canada.	February 1994
12.	Lipid vesicles and the regression of atherosclerosis	Canadian Lipoprotein Research Conference, Whistler, BC, Canada	April 1994
13.	Cationic lipids and gene delivery	Annual Meeting, Canadian Genetic Diseases Network, Parksville, Vancouver Island, BC, Canada	May 1994
14.	Pharmaceutical formulation and development of liposomal ciproflaoxacin	Bayer Canada, Toronto, ON, Canada	April 1995
15.	Liposomes and the management of atherosclerosis	Parke-Davis Pharmaceuticals, Ann Arbor, MI, USA	October 1995
16.	Delivery of antisense oligonucleotides	Dermatology 2000, Vancouver, BC, Canada	May 1996
17.	Strategic partnering in biotechnology	Vancouver Enterprise Forum, Science World, Vancouver, BC, Canada	May 1996
18.	Non-viral gene delivery	Canadian Society of Investigative Dermatology, Whistler, BC, Canada	June 1996
19.	Intracellular drug delivery	Canadian Society of Microbiologists, Charlottetown, PEI, Canada	June 1996
20.	Antisense drug delivery	B.C. Cancer Agency, Vancouver, B.C. Canada	July 1997
21.	Antisense drug delivery	Antisense technology, San Francisco, US	June 1998
22.	Antisense drug delivery	Antisense 98, London, UK	October 1998

#	TITLE	LOCATION	DATE
23.	Antisense drug delivery	Leukemia Society Workshop, Philadelphia, US	October 1999
24.	Antisense drug delivery	TIDES Conference, Tucson, US	April, 2001
25.	Oligonucleotide delivery and immune stimulation	LongBranch, New Jersey, US	February, 2002
26.	Liposomal delivery of antisense and conventional drugs	Pharmacia, St. Louis, MS, US	June, 2002
27.	Oligonucleotide delivery and immune stimulation	Membrane Research Conference, Davos, Switzerland	October, 2002
28.			
29.			
30.			

Other Presentations

Numerous presentations to pharmaceutical companies

Other

Conference Participation (Organizer, Keynote Speaker, etc.)

Co-Organizer, 1985 Western Canada, Biomembranes Conference, Vancouver, BC, Canada.

Memberships on scholarly societies, including offices held and dates

British Biochemical Society (Member)
American Chemical Society (Member)
American Association of Cancer Research (Member)
American Association of Immunologists (Member)

Memberships on scholarly committees, including offices held and dates

Member of Scholarship Evaluation Committee, Science Council of B.C. 1996 -

Editorships (list journal and dates)

Co-Editor of Special Issue of Chemistry and Physics of Lipids, "Liposomes" Vol. 40, p. 87-401, 1986
Asst. Editor Antisense and Nucleic Acid Drug Development

Reviewer (journal, agency, etc. including dates)

Reviewer for the following journals and agencies:

1. Regular Reviewer for Biochimica Biophysica Acta
2. Biochemistry
3. Chemistry and Physics of Lipids
4. Journal of Liposomology
5. Journal of Investigative Dermatology
6. Journal of Biochemistry and Biology
7. Journal of Lipid Research

8. Journal of Analytical Biochemistry
9. Peer reviewer for National Research Foundation
10. Peer reviewer for Canadian Heart & Stroke Foundation
11. Peer reviewer for B.C. Science Council
12. Peer reviewer for NIH

Consultant (indicate organization and dates)

1.	Consultant, The Liposome Company, Inc., Princeton, N.J.	(1984 - 1987)
2.	Founder, Treasurer and Director - Lipex Biomembranes Inc.,Vancouver	(1986 - present)
3.	Vice President, The Canadian Liposome Co. Ltd.	(1987 - 1991)
4.	Founder and President - Applied Lipid Systems Ltd	(1991 -1992)
5.	Director and Principal Investigator, Liposome Research Unit	(1991 - present)
6.	Director and Principal Investigator, Skin Barrier Research Program	(1991 - present)
7.	Consultant Johnson & Johnson Pharmaceuticals	(1991 - 1993)
8.	Consultant Ault Foods Inc	(1990 - 1993)
9.	Founder and Director Drug Delivery, INEX Pharmaceuticals Corp.	(1992 - present)

Awards for Scholarship (indicate name of award, awarding organizations, date)

Science Research Council Studentship Award, 1973 - 1976
Dutch Ministry of Education Science Scholarship, 1976 - 1977
European Molecular Biology Organization Fellowship, 1977 - 1978

BOOKS

Chapters

1. Cullis, P.R., Hornby, A.P. and **Hope, M.J.** "Effects of anaesthetics on lipid polymorphism" in: Molecular Mechanisms of Anaesthesia - Progress in Anaesthesiology. Vol. 2, (B.R. Fink, Ed.) Raven Press, 1980
2. de Kruijff, B., Verkleij, A.J., van Echteld, C.J.A., Gerritsen, W.J., Noordam, P.C., Mombers, C., Rietveld, A., de Gier, J., Cullis, P.R., **Hope, M.J.** and Nayar, R. "Nonbilayer lipids in the inner mitochondrial membrane" Cell Biology 1980-1981 (H.G. Schweiger, Ed.) Springer-Veriag Berlin, pp 559-571, 1981
3. Cullis, P.R., de Kruijff, B., **Hope, M.J.**, Verkleij, A.J., Nayar, R., Farren, S.B., Tilcock, C.P.S., Madden, T.D. and Bally, M.B. "Structural properties of lipids and their functional roles in biological membranes" in: Membrane Fluidity in Biology Vol. 2(R.C. Akloia, Ed.) Academic Press, N.Y., 1982
4. Verkleij, A.J., van Venetie, R., Leunissen-Bijvelt, J., de Kruijff, B., **Hope, M.J.** and Cullis, P.R. "Membrane fusion and lipid polymorphism" in: Physical Methods on Biological Membranes and their Model Membranes (F. Conti. Ed.) Plenum Press N.Y., 1984
5. de Kruijff, B., Cullis, P.R., Verkleij, A.J., **Hope, M.J.**, van Echteld, C.J.A. and Taraschi, T.F. "Lipid Polymorphism and Membrane Fusion", in Enzymes of Biological Membranes (A. Martinosi,ed.) Plenum Press, N.Y., pp. 131-204, 1984
6. Cullis, P.R., **Hope, M.J.**, Nayar, R., Bally, M.B. and Tilcock, C.P.S. "Roles of Phospholipids in Exocytosis" in: Phospholipids in the Nervous System, Vol. 2: Physiological Roles (L. Horrochs et al, ed.) Raven Press, New York pp 71-86, 1985
7. Cullis, P.R. and **Hope, M.J.** "Physical Properties and Funcional Roles of Lipids in Membranes" in: Biochemistry of Lipids and Membranes (D.E. Vance and J.E. Vance, Eds) Benjamin Cummings, Menio Park pp.25-72, 1985
8. Cullis, P.R., **Hope, M.J.**, de Kruijff, B., Verkleij, A.J. and Tilcock, C.P.S. "Structural Properties and Funcional Roles of Phospholipids in Membranes, in: Phospholipids and Cellular Regulation (J.F.Kuo, Ed.) CRC Press, Boca Raton, Ch.1, pp.1-60, 1985
9. Cullis, P.R., **Hope, M.J.**, Bally, M.B., Janoff, A.S., Madden, T.D. and Mayer, L.D. "Liposomes as Pharmaceuticals" in: Liposomes (M. Ostro, Ed.) Marcel Dekker, N.Y. pp. 39-72, 1987
10. Bally, M.B., **Hope, M.J.**, Mayer, L.D., Madden, T.D. and Cullis, P.R. "Novel procedures for generating and loading liposomal systems" in: Liposomes as Drug Carriers (G. Gregoriadis, ed.) John Wiley and Sons, N.Y., pp. 841-853, 1988
11. Cullis, P.R., **Hope, M.J.** and Tilcock, C.P.S. "Lipid Polymorphism" in Cellular Membrane Fusion (J. Wilschut and D. Hoekstra,Eds) Marcel Dekker Inc., New York, 35-64,1990
12. Cullis, P.R. and **Hope, M.J.** "Physical Properties and Funcional Roles of Lipids in Membranes" in: Biochemistry of Lipids and Membranes (D.E. Vance and J.E. Vance, Eds) Elsevier, Amsterdam, New Comprehensive Biochemistry, vol. 20, pp 1-41 (1991)
13. **Hope MJ**, Nayar R, Mayer LD, Cullis PR. Reduction of liposome size and preparation of unilamellar vesicles by extrusion. in Liposome Technology, vol 1, 2nd edition (G. Gregoriadis, Ed) CRC Press p 123-139 (1992)
14. Bally MB, Mayer LD, **Hope MJ**, Nayar R. Pharmacodynamics of liposomal drug carriers: methodological considerations. in Liposome Technology, vol 3, 2nd edition (G. Gregoriadis, Ed.) CRC Press, p 27-41 (1992)
15. **Hope, M.J.,** Rodrigueza, W.V. "Freeze fracture of model membranes", in: Techniques in Modern Biomedical Microscopy, N.J. Severs and D.M. Shotton, Eds., Wiley-Liss, Inc., 235-253, (1995)
16. **Hope, M.J.** and Wong, K. "Liposomal formulation of Ciprofloxacin" in: Liposomes in Biomedical Applications, P. Shek, Ed., 121-134, (1995)
17. Cullis, P.R., Fenske, D.B. and **Hope, M.J.** "Physical Properties and Funcional Roles of Lipids in Membranes" in: Biochemistry of Lipids,Lipoproteins and Membranes (D.E. Vance and J.E. Vance, Eds) Elsevier Sciences, Amsterdam, New Comprehensive Biochemistry, vol. 31, pp 1-33 (1996)

18. Fenske, D., Monck, M.A., **Hope, M.J.** and Cullis, P.R. "The Functional Roles of Lipids in Biological Membranes", in: Biomembranes, Vol. 1, JAI Press, in press (1997)

4. PATENTS

1. Formulation of ribozyme against VEGF-flt1 receptor showing enhanced antitumor activity in vivo. July 97. Inventors: **M.J. Hope**, S. Semple, P. Scherrer, M. Reynolds, J. Min.
2. Novel method for high efficiency encapsulation of oligonucleotides. May 97. Inventors: S. Semple, **M.J. Hope**, P.R. Cullis, S. Klimuk, P. Scherrer.
3. Method of dehydrating liposomes using protective sugars. US 5578320. Nov. 26, 1996. Granted and filings in 15 countries. Inventors: A.S. Janoff, P.R. Cullis, M.B. Bally, M.W. Fountain, R.S. Ginsberg, **M.J. Hope**, T.D. Madden, H.P. Schieren, R.L. Jablonski.
4. Enhanced efficacy of liposomal antisense. May 96. Inventors: S. Klimuk, S. Semple, P. Scherrer, **M.J. Hope**.
5. Methods for encapsulating Plasmids in Lipid Bilayers. Jun. 95. Inventors: J. Wheeler, **M.J. Hope**, P.R. Cullis, M.B. Bally.
6. Method for loading lipid vesicles. Feb. 95. Inventors: **M. J Hope**, P.R. Cullis, D. Fenske, K. Wong.
7. Novel compositions for the introduction of polyanionic materials into cells. 1 October 94. Inventors: S. Ansell, B. L.-S. Mui, **M.J. Hope**.
8. Liposomal composition for the treatment of atherosclerosis. US serial no 08/206,415. 4 March 94. Inventors: **M.J. Hope**, W.V. Rodrigueza.
9. Labeled liposomes methods and uses. US serial no 08/159,183. November 30, 1993. Inventors: **M.J. Hope**, L. Ahkong.
10. Liposomes having defined size distributions. US serial no. 659,104. 21 February 91. Inventors: **M.J. Hope**, M.B. Bally, P.R. Cullis.
11. Accumulation of drugs linto liposomes by a proton gradient. EP 0472639. 15 May 90. Inventors: T.D. Madden, **M.J. Hope**, C.P.S. Tilcock, P.R. Cullis, P.R. Harrigan, B. L.-S. Mui, M.B. Bally, L. Tai, L.D. Mayer.
12. Extrusion technique for producing unilamellar liposomes. US 5008050. 13 February 89. Granted and five additional countries. Inventors: P.R. Cullis, **M.J. Hope**, M.B. Bally.
13. Encapsulation of antineoplastic agents in liposomes. US 5077056. 12 December 88. Granted and six more in five countries. Inventors: P.R. Cullis, **M.J. Hope**, T.D. Madden.
14. Induction of asymmetry in vesicles. CA 1307738. 12 June 87. Granted and 15 other countries. Inventors: **M.J. Hope**, P.R. Cullis.
15. Solubilization of hydrophobic materials using phospholipids. US 4923854. 22 January 86. Granted and twelve other countries. Inventors: A.S. Janoff, P.R. Cullis, M.B. Bally, R.S. Ginsberg, **M.J. Hope**, T.D. Madden, H.P. Schieren, R.L. Jablonski.

5. REFERENCES

1. MUI, B., RANEY, S. G., SEMPLE, S. C., HOPE, M. J.: Immune stimulation by a CpG-containing oligodeoxynucleotide is enhanced when encapsulated and delivered in lipid particles. J Pharmacol. Exp. Ther. **298,** 1185-1192, **2001**.
Ref ID: 30204

2. SEMPLE, S. C., KLIMUK, S. K., HARASYM, T. O., DOS, S. N., ANSELL, S. M., WONG, K. F., MAURER, N., STARK, H., CULLIS, P. R., HOPE, M. J., SCHERRER, P.: Efficient encapsulation of antisense oligonucleotides in lipid vesicles using ionizable aminolipids: formation of novel small multilamellar vesicle structures. Biochim Biophys Acta **1510,** 152-166, **2001**.
Ref ID: 30206

3. BRAMSON, J. L., BODNER, C. A., JOHNSON, J., SEMPLE, S., HOPE, M. J.: Intravenous administration of stabilized antisense lipid particles (SALP) leads to activation and expansion of liver natural killer cells. Antisense Nucleic Acid Drug Dev. **10,** 217-224, **2000.**
Ref ID: 30040

4. KLIMUK, S. K., SEMPLE, S. C., NAHIRNEY, P. N., MULLEN, M. C., BENNETT, C. F., SCHERRER, P., HOPE, M. J.: Enhanced anti-inflammatory activity of a liposomal intercellular adhesion molecule-1 antisense oligodeoxynucleotide in an acute model of contact hypersensitivity. J Pharmacol Exp Ther **292,** 480-488, **2000.**
Ref ID: 29718

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